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(54) Title: METHODS FOR PRODUCING TRANSGENIC ANIMALS

(57) Abstract: The present invention relates to methods for producing transgenic animals. Specifically, the methods of the present invention include production of a transgenic animal by transgenic intracytoplasmic sperm injection, retroviral gene transfer, intracytoplasmic nuclear injection, and pronuclear injection. In addition, the present invention also relates to methods for using transgenic animals as models for human disease and diagnosis. In particular, these transgenic animals may be used as models for embryo and fetal development, as models to assess the safety and efficacy of drug therapy and gene therapy, and as models for disease diagnosis. The methods of the present invention are also directed to methods of using transgenic embryonic cells to treat human diseases.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/34011

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01K67/027 A61K49/00 C12N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PERRY A ET AL: "Mammalian transgenesis by intracytoplasmic sperm injection" SCIENCE., vol. 284, 14 May 1999 (1999-05-14), pages 1180-1183, XP000919050 cited in the application	1,2, 5-19, 22-32, 36-42
Y	figure 2; table 2	3,4,44, 47-64
Y	HEWITSON L ET AL: "Unique checkpoints during the first cell cycle of fertilization after intracytoplasmic sperm injection in rhesus monkeys" NAT MED, vol. 5, no. 4, April 1999 (1999-04), pages 431-433, XP002168953 cited in the application figure 1	3,4,45, 46
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/34011

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 41615 A (WISCONSIN ALUMNI RES FOUND) 24 September 1998 (1998-09-24) cited in the application examples 6,7 ---	44-64
P,X	WO 00 09674 A (UNIV HAWAII) 24 February 2000 (2000-02-24) the whole document ---	1-43,79
P,X	WO 00 08924 A (PERRY ANTHONY C F ;WAKAYAMA TERUHIKO (US)) 24 February 2000 (2000-02-24) the whole document ---	1-43,79
P,X	CHAN A ET AL: "Foreign DNA transmission by ICSI: injection of spermatozoa bound with exogenous DNA results in embryonic GFP expression and live rhesus monkey births" MOL HUM REPROD, vol. 6, no. 1, January 2000 (2000-01), pages 26-33, XP001002490 cited in the application the whole document ---	1-43,79
A	WO 99 25863 A (HOVATTA OUTI ;WINSTON ROBERT (GB); IMPERIAL COLLEGE (GB); CEDARS S) 27 May 1999 (1999-05-27) page 9, line 2; claims 19,31 ---	1,44,75
A	WO 97 45531 A (WISCONSIN ALUMNI RES FOUND ;HEARN JOHN PATRICK (US)) 4 December 1997 (1997-12-04) ---	
A	WO 94 19455 A (GENENTECH INC ;OREGON MEDICAL RES FOUND (US)) 1 September 1994 (1994-09-01) ---	
A	EP 0 867 114 A (IWAYA MAKOTO ;OGAWA SHYOSO (JP); HOECHST MARION ROUSSEL LTD (JP)) 30 September 1998 (1998-09-30) ---	
A	SIMONI M: " Transgenic animals in male reproduction research" EXPERIMENTAL AND CLINICAL ENDOCRINOLOGY, vol. 102, no. 6, pages 419-433, XP001002682 ---	
T	CHAN A ET AL: "Transgenic monkeys produced by retroviral gene transfer into mature oocytes" SCIENCE., vol. 291, no. 5502, 12 January 2001 (2001-01-12), pages 309-312, XP002168955 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/34011

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see further information sheet invention 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-64, 75,
79 (all totally) and 76-78 (all partially)

- 1.1. Claims: 1-43,
79 (all totally) and 76-78 (all partially)

Method for producing a transgenic animal comprising the step of transferring exogenous DNA by intracytoplasmic sperm injection into an oocyte; wherein said exogenous DNA is bound to the spermatozoon.

- 1.2. Claims: 44-64 (all totally) and 76-78 (all partially)

Method for producing a transgenic animal comprising the step of transferring exogenous DNA by intracytoplasmic sperm injection into an oocyte, wherein said exogenous DNA is provided as a retroviral particle.

- 1.3. Claims: 75 (totally) and 76-78 (all partially)
Method for producing a transgenic animal comprising the step of transferring exogenous DNA by intracytoplasmic sperm injection into an oocyte, wherein said exogenous DNA is provided by pronuclear injection.

2. Claims: 65-69 (all totally) and 76-78 (all partially)

Method for producing a transgenic primate comprising the step of injecting a nucleus into an enucleated oocyte by intracytoplasmic nuclear injection, wherein said nucleus is isolated from a blastomere

3. Claims: 70-74 (all totally) and 76-78 (all partially)

Method for producing a transgenic primate comprising the step of injecting a nucleus into an enucleated oocyte by intracytoplasmic nuclear injection, wherein said nucleus is isolated from a somatic cell.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/34011

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9841615 A	24-09-1998	US 6080912 A	27-06-2000
		AU 6472398 A	12-10-1998
		CA 2254866 A	24-09-1998
		EP 0909313 A	21-04-1999
WO 0009674 A	24-02-2000	AU 5475299 A	06-03-2000
		AU 5560399 A	06-03-2000
		EP 1105469 A	13-06-2001
		EP 1111991 A	04-07-2001
		WO 0008924 A	24-02-2000
WO 0008924 A	24-02-2000	AU 5475299 A	06-03-2000
		AU 5560399 A	06-03-2000
		EP 1105469 A	13-06-2001
		EP 1111991 A	04-07-2001
		WO 0009674 A	24-02-2000
WO 9925863 A	27-05-1999	AU 1406199 A	07-06-1999
		EP 1030929 A	30-08-2000
WO 9745531 A	04-12-1997	US 5824548 A	20-10-1998
		AU 2908097 A	05-01-1998
		US 6110741 A	29-08-2000
WO 9419455 A	01-09-1994	US 5563059 A	08-10-1996
		AU 672103 B	19-09-1996
		AU 6249794 A	14-09-1994
		CA 2154447 A	01-09-1994
		EP 0686192 A	13-12-1995
		JP 8507211 T	06-08-1996
		US 5693534 A	02-12-1997
EP 0867114 A	30-09-1998	JP 10304790 A	17-11-1998
		AU 707361 B	08-07-1999
		AU 7096796 A	17-04-1997
		CA 2233694 A	03-04-1997
		WO 9711597 A	03-04-1997